UPDATED 4TH EDITION

"The definitive resource for every celiac, those yet to be diagnosed, and their families."
—CELIAC DISEASE FOUNDATION

Celiac Disease

A HIDDEN EPIDEMIC

Is Gluten Making You Sick?

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Introduction

What's Wrong with Me?

"My doctor kept treating my symptoms, but never figured out why my stomach was always upset. I started getting migraines and then joint pain and.... well, you name it. I was a walking pharmacy and still felt lousy". (Marg, 47)

"My daughter was always tired. It was a joke with her friends—where's Mel—she's asleep. She slept through classes in college.... it affected her social life. We even did an overnight sleep study in the hospital—she was sleeping fourteen to sixteen hours a day". (Roni)

"My daughter had legs like pick-up sticks and an enormous belly and the pediatrician called it "baby fat" and said she'd grow into it". (Mike, 40)

"I think people thought I was a hypochondriac—there was so much wrong with me". (Heather, 43)

In the United States today, millions of patients suffer with symptoms that neither fit a specific diagnosis nor disappear. Young and old take drugs and see numerous specialists for gastrointestinal complaints, anemia, joint pain, itchy skin conditions, constant fatigue, or headaches. Their symptoms are treated, but no underlying cause can be found. One doctor diagnoses fibromyalgia, another chronic fatigue syndrome, a third irritable bowel syndrome. Too much or too little roughage, lactose or fructose intolerance, fried or spicy food explains repeated bouts of reflux, diarrhea, constipation, abdominal pain, and gas. Muscle strain or the "wrong type of mattress" is the excuse for aching joints or tingling extremities that remain asleep when the rest of you wakes up in the morning.

Frustrated, patients seek care from "alternative" nontraditional physicians because a friend or neighbor got help there or the physician appeared on TV. Hundreds of dollars later—after a battery of blood or stool tests that most traditional physicians will not even review once they see the name of the laboratory that performed them—the diagnosis comes down to "leaky" gut or too much of the wrong bacteria. Trials of antibacterial agents, expensive intravenous vitamin infusions, multiple herbal remedies, or low-yeast diets all seem the answer. They provide a temporary respite when well-trained physicians cannot provide an answer. Six or seven years into this downward physical and mental spiral, an internist suggests that stress may be the answer. In other words, we cannot find anything really wrong with you—perhaps it is "in your head." Many patients live in a perpetual state of indefinable ill health that, after a period of time, they begin to accept as normal. Some of the symptoms seem to "run in the family.

" I've had it (reflux and dyspepsia) for so long that I just think it's a normal part of my life. My mother has it, my brother has it. So, I just assume it's what I'm supposed to have". (Cindy, 45)

For many patients, there is a medical diagnosis for the bundle of symptoms they must endure. Diagnosis and treatment of this condition will not only improve your health, it may save your life.

The Celiac Iceberg

Celiac disease is a multisystem disorder whose primary target of injury is the small intestine. The disease is triggered by gluten, the main storage protein found in certain grains. Gluten damages the small intestine so that it is unable to absorb nutrients properly. As food malabsorption continues and the disease progresses, the manifestations inevitably become more varied and complex. Celiac disease is the most common—and one of the most underdiagnosed—hereditary autoimmune condition in the United States today. It is as common as hereditary high cholesterol. Once considered a rare "diarrheal" disease of childhood, celiac disease is now recognized predominantly as a disease of adults—and the majority of people are either asymptomatic or

consult doctors for a variety of other complaints. While the disease is considered common in Europe, South America, Canada, and Australia—a recent study of schoolchildren in Finland showed the incidence to be one per ninety-nine, in parts of England one per one hundred—only recently have studies shown that celiac disease affects approximately 1 percent of the U.S. population (approximately 1 in every 100 people)—and about 50 percent of them are undiagnosed.

Unfortunately, if the disease progresses and is not diagnosed until later in adulthood, patients often develop many other problems from years of inflammation and the malabsorption of minerals, vitamins, and other necessary nutrients. A delay in diagnosis also increases the chances of developing associated autoimmune diseases. Most adults with celiac disease have bone loss, resulting in osteopenia or osteoporosis. Anemia, malignancies, peripheral neuropathies (numb and/or tingling extremities), dental enamel defects, hyposplenism (underactive spleen), and infertility are also secondary conditions associated with the disease. Since patients with one autoimmune disease are more likely to have or to develop another, patients with celiac disease are also seen with Sjögren's syndrome, type 1 diabetes, autoimmune thyroid disease, dermatitis herpetiformis (an intensely itchy skin condition), or alopecia areata (a condition that causes hair loss). Of the 1.25 million people with type 1 diabetes, 8 to 10 percent also have celiac disease. Often, people are treated for an autoimmune condition before being diagnosed with celiac disease.

Unfortunately, there is an increased mortality rate for people with celiac disease, exceeding that of the general population, due mainly to malignancies. Current research shows a statistical risk that is 33 times greater for small intestinal adenocarcinoma, 11.6 times greater for esophageal cancer, 9.1 times greater for non-Hodgkin's lymphoma, 5 times greater for melanoma, and 23 times greater for papillary thyroid cancer. In the United States today, the diagnosis of celiac disease can take five to seven years. Patients normally see numerous physicians and specialists for symptoms that are misdiagnosed, do not respond to drug therapy, or are treated without concern for their underlying cause. Young children may suffer for one-third to one-half their lifetime before obtaining a diagnosis. A majority of people in the United States have a "silent" variety of celiac disease. Without marked gastrointestinal symptoms, many of these patients are diagnosed with celiac disease concurrent with another diagnosis, often a malignancy. This scenario also occurs in adults who received a celiac disease diagnosis as a child and whose parents were told they would "grow out of it."

"I was told by my mom—many, many years ago—that I had celiac disease as a baby. I had severe diarrhea and the doctor put me on a special milk and bananas diet and it went away and that was the end of it. When I was diagnosed with celiac disease two years ago, I said: "I had that as a baby". (Linda, 62)

You do not outgrow celiac disease. You develop symptoms that point in other medical directions and become part of the iceberg that is "below the waterline" and off the medical radar screens. Patients often see doctors for a myriad of other complaints, and their mild or apparently unrelated symptoms are often only recognized retrospectively.

"Why Worry?"

Celiac disease is a significant medical condition. It is far too often masked by or mistaken for a number of more commonly diagnosed conditions. The result is a huge population of patients suffering unnecessarily and at considerable risk for major complications. These patients may also be burdened by depression and complicated professional and family dynamics as a result of their long-term undiagnosed illnesses. Recent research and educational efforts have markedly increased the number of people who are diagnosed with celiac disease. Our efforts now must also concentrate on quality of life—to ensure that those with celiac disease remain happy and healthy. Celiac disease is a huge iceberg that is moving, not quite so silently, across many of our lives.

Part I Is the Food You Eat Eating You?

1- Normal Digestion

Gas, burps, stomachaches, and bloating are standard fodder for comedy routines—because of their frequency as much as the discomfort and embarrassment they cause. Digestive disorders are among the most common problems we experience. Recent figures show that almost half the U.S. population experiences heartburn regularly, one in five are lactose intolerant, and colon and rectal cancers are second only to lung cancer as a leading cause of cancer deaths. In order to understand the impact of a malfunction in the digestive tract and why it leads to all of the symptomatic manifestations of celiac disease, it is necessary to understand how the body normally digests and absorbs food.

“Food keeps my body running and it keeps me up at night”. (Gary, 49)

The digestive system has been described as the outside world going through us. Designed to supply the body with all of the nutrients and fluids it needs to function, it is essentially a long tube that is open at both ends. Food enters at one end, the nutrients the body can use are absorbed by the lining of the gastrointestinal tract, and nondigested residue is excreted from the other end. The concept is simple, the design and execution quite remarkable.

The Gastrointestinal (GI) Tract

Food enters the GI tract via the mouth; moves through the pharynx, esophagus, stomach, small intestine (the duodenum, jejunum, and ileum), and large intestine (colon); and exits from the anus. The salivary glands, pancreas, liver, and gallbladder are organs that secrete the enzymes and fluids that help digest food. They are connected to the digestive system by ducts. The digestive system, or gut, is intimately related to the following:

- The circulatory system, which transports the nutrients from the intestine to the tissues throughout the body and liver.
- The enteric nervous system, which helps control enzyme release and muscular contractions of the gut.
- The muscles of the digestive system, which provide motility to help digest and move food through the long tract.

If one section of the system malfunctions, it almost necessarily affects another, and there are numerous places for things to go wrong.

Digestion

Digestion is the word commonly used to describe a three-part process:

- Digestion—the breakdown of food products into ever smaller and smaller components that can be absorbed
- Absorption—the passage of food products that have been broken down into the intestinal wall
- Transport—the transfer of food from the intestinal wall to the cells of the body

Digestion requires the following:

- The chemical breakdown of food by enzymes
- The mechanical mixing and propulsion of the products of chemical activity by the intestinal muscle.

Digestion actually begins before the food even enters your mouth. When you see, think about, or smell food, the vagus nerve transmits a chemical message from your brain to release saliva in the mouth, increase stomach motility, and release gastric acid in the stomach. We begin to salivate and the stomach “rumbles” at the very anticipation of food.

The Mouth

In the mouth, chewing tears the food apart and grinds it into smaller components. Saliva, a mucous substance, is secreted to lubricate and start to dissolve the food. It contains various enzymes that start the digestion of fats and carbohydrates that are continued farther down the digestive tract. Saliva also acts as a glue to hold the food together as it travels toward the stomach. We swallow the ball, or bolus, of chewed food and saliva, and it is transported down our esophagus. While the skeletal muscles at work in the mouth and throat are voluntary—we consciously move our jaws and swallow—smooth muscles that function involuntarily take over in the esophagus. The gut actually has its own pacemaker. An undulating contraction of muscles called peristalsis begins and moves the food into the stomach where the action, quite literally, really starts.

The Stomach

The stomach is a big muscular sac or reservoir that holds the chewed food until it is ready to move on, mixes it with gastric juices, and starts many of the chemical processes of digestion. The muscular movements of the stomach act like a Cuisinart—chopping, blending, and mixing the ball of food to form a soupy puree called chyme. The stomach secretes an enormous amount of gastric acid, which functions to both break down the food and convert the stomach into a disinfecting tank, killing bacteria and inactivating toxins in the food we have eaten. Pepsin, an enzyme secreted by the stomach, starts the digestion of protein. The stomach also sends messages (in the form of hormones) to the other digestive organs telling them that food has arrived. This stimulates the secretion of pancreatic juices and bile from the liver and gallbladder that will further break down the chyme once it moves into the small intestine. The only substances that are absorbed directly into the bloodstream in the stomach are aspirin and alcohol.

One-Way Street

The sphincters that connect the esophagus to the stomach and the stomach to the small intestine are one-way valves. Food is only meant to travel down the GI tract—a street sign that is often ignored. Occasionally, chyme refluxes, or backs up, into the esophagus—a condition known as GERD, gastroesophageal reflux disease—and the gastric acid becomes a corrosive agent on the less well-protected lining of the esophagus. (See Chapter 3.) When the chyme is sufficiently liquefied, muscle/peristaltic contractions gradually push it into the upper part of the small intestine, the duodenum. The stomach empties in a slow and controlled way so as not to overwhelm all the mechanisms of digestion in the small intestine. As the small intestine fills with chyme, it signals the stomach to decrease its activity and slow down the emptying process. This is one reason a large meal “stays with you”; i.e., it lingers in the stomach until the small intestine can process it. The arrival of chyme in the small intestine triggers the release of specific hormones that stimulate the release of enzymes and fluids into the lumen, the center of the tube, to facilitate digestion. The pancreas and the liver supply many of these enzymes and fluids that break down food into components small enough to be absorbed. They are regulated by both the nervous system and gastrointestinal hormones. Their secretions are called for only when needed by the digestive system.

The Pancreas

In addition to its endocrine function (the production of insulin), the pancreas produces enzymes such as trypsin, which breaks down proteins; amylase, which breaks down starches; and lipase,

which breaks down fats. When the pancreas becomes inflamed or diseased (e.g., pancreatitis), these enzymes are not secreted and, as a result, carbohydrate, protein, and fat digestion is impaired. (See Pancreatic Insufficiency, Chapter 16.)

The Liver

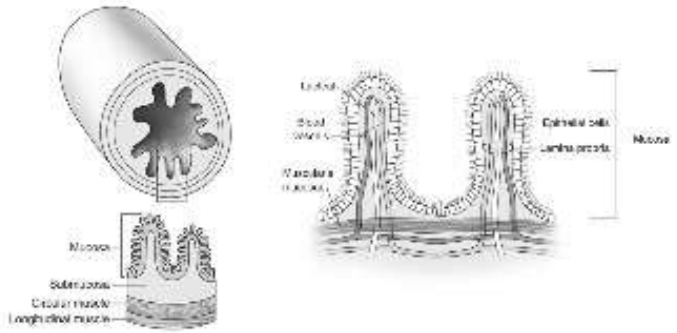
The liver plays an important role in the metabolism, transport, and storage of nutrients. It assists in the digestion of fats by secreting bile, which increases the solubility of fats, enabling them to pass through the intestinal wall into the bloodstream. The bile produced by the liver is stored in the gallbladder until needed; it is delivered to the small intestine on the arrival of fatty foods, which stimulate its release. The many chemical messengers that stimulate the digestive organs are balanced by a feedback mechanism that turns off production. This delicate balance, or homeostasis, controls all digestive functions.

The Small Intestine

The small intestine is the major site for both the digestion (breaking down) and absorption of nutrients. In the average adult, it is approximately twenty-two feet long and consists of three parts:

- The duodenum (the first segment)
- The jejunum (the second segment—together with the duodenum known as the proximal intestine)
- The ileum (the third segment or distal intestine)

All three segments have similar anatomy, but each has a specific job, digesting and absorbing particular nutrients. While digestion takes place in the lumen of the small intestine, absorption occurs through the lining or mucosal wall of the intestine, which has a unique structure. The twenty-two feet of small intestine actually possesses a much larger surface area than it would appear. The lining of the wall of the small intestine, the mucosa, consists of folds that markedly increase its surface area. The folds are in turn covered with tiny fingerlike projections, or villi, that contain the cells that absorb nutrients. These villi further amplify the surface area.



Figures 2 and 3. A Cross Section of the Intestinal Wall

The surface of each villus has a “brushlike” border consisting of microvilli, or tiny hairs, that increase the absorptive surface of the small intestine yet again. The brush border also contains enzymes that are necessary for the digestion of specific food components. If you were to flatten out the intestinal mucosa—all the villi, microvilli, and crypts (the small valleys between each villus)—the “small” intestine actually has a surface area about the size of a tennis court that is totally dedicated to absorbing food! This enormous capacity ensures that the intestine can sustain a fair amount of assault and/or damage and still feed the body. Inflammatory cells normally inhabit the mucosa to protect the small intestine against toxins and bacteria. Since the food supply entering the GI tract is not “sterile” and may contain toxic substances, these white blood cells are the first line of defense. This results in a state of constant controlled inflammation in the mucosa. (See The Burn, Chapter 3.)

The Villi

The villi are the workhorses of the intestine. They are the final intestinal link between your dinner plate and your bloodstream. And this is where celiac disease does its primary damage. The villi play a crucial role by:

- Dramatically increasing the surface area of the small intestine to allow the absorption of food.
- Releasing enzymes that continue and complete the breakdown/digestion of food.
- Absorbing the products of digestion and transporting them into the bloodstream for distribution throughout the body.
- Acting as a barrier that blocks bacteria, parasites, and toxins from entering the body.

Each villus is an independent, but intimately related part of the assembly line. The villi are made up of epithelial cells that cover a core containing blood and lymph vessels, nerve fibers, and a muscle layer. As illustrated in Figure 2, the muscle is both longitudinal (pushing) and circular (mixing). This muscular component consists of smooth muscle that is innately contractile. It is a crucial aspect of digestion, since contractions of the smooth muscle both propel and mix the chyme as it travels down the digestive tract. Without peristalsis, there would be no digestion. It is important to understand that the final stages of digestion, absorption, and transport of nutrients occur through—not between—these tiny, fingerlike projections. When there is inflammation, and a breakdown of the lining of the intestine, the bowel may become “leaky.”

This enables whole molecules of food and/or toxins to get between or through the epithelial cells, interrupting their protective function. When the lining is intact, larger molecules will not enter the bowel wall and bloodstream. There are millions of these microscopic villi in each section of the small intestine. Because of its enormous capacity to absorb, parts of it can be damaged with no obvious manifestations or symptoms. This enormous anatomical surplus is designed to compensate for damage to the intestine from any source, infection, poison, or inflammation. But when large sections of the lining are inflamed or destroyed, absorption, enzyme release, transport of nutrients to the body, and the defensive ability of the small intestine are compromised.

Crypts

The small valleys between the villi—crypts—continuously produce and replace the absorptive epithelial cells lining each villus of the GI tract and secrete enzymes into the lumen to aid in digestion. Billions of epithelial cells are replaced every day, but if the villi are inflamed or damaged, new cells are unable to work their way up the villus and the crypts become swollen.

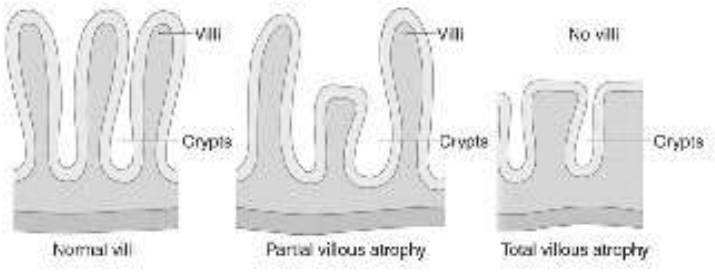


Figure 4. Normal Villi; Partial Villous Atrophy; Total Villous Atrophy

Absorption

Once the food components traveling through the lumen are sufficiently digested (broken down), they are absorbed by different parts of the small intestine. A disease of or infection in one section of the small intestine is often revealed by the malabsorption of specific nutrients. Iron deficiency and metabolic bone disease (e.g., osteoporosis or osteopenia) occur when disease involves the proximal intestine. Fat and sugars also get absorbed in the upper intestine. If they are

malabsorbed, and the ileum cannot compensate, they get into the colon and you get diarrhea. (See Chapter 3.) Vitamin B12 malabsorption occurs when the ileum is involved in a disease process. This may occur in severe celiac disease or, more commonly, Crohn's disease with ileitis. Unless there is a disease process at work, the absorption process works efficiently and steadily until every usable nutrient in the chyme is absorbed. Limits are placed only on the absorption of necessary, but potentially toxic minerals such as iron and calcium.

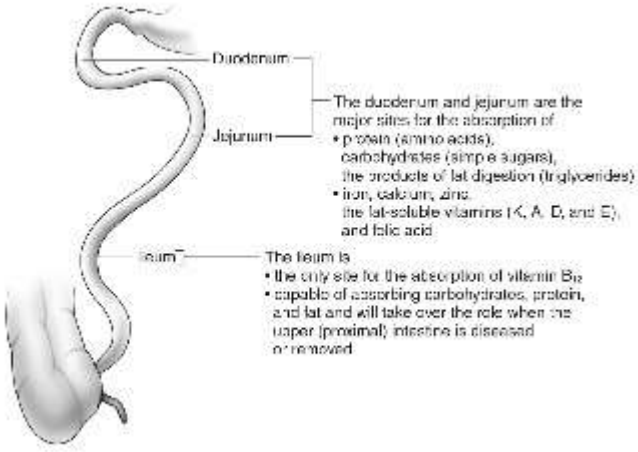


Figure 5. Absorption Sites in the Small Intestine

If we eat more than the body needs for energy and efficient cellular function, the nutrients are absorbed and stored—primarily as body fat. The digestive system is designed for survival, and this function can outsmart any diet that supplies more food than the body needs at a given time.

Transport

Once the food components are actively absorbed by the intestinal wall, they are transported into the body. Carbohydrates, protein, and fat are taken up (absorbed) from the lumen and transported across the epithelial cell membranes by different mechanisms. Some food components move across quite easily while others require specialized chemical "porters" that literally bind to the components and "carry" them across the cells of the villi. The villi are full-service providers. They not only supply the enzymes and fluids that break down specific foods, they supply the "porters" that enable the food components to enter the body.

Carbohydrates

Carbohydrates supply the body with the fuel it requires for immediate as well as long-term muscle function and energy. The simple sugars are readily transported across the villi into the bloodstream.

Proteins

Proteins are the building blocks of the body, an essential part of every cell, organ, and system. They are made up of amino acids that are usually strung together in "chains" and held together by peptide bonds. Enzymes secreted by the pancreas and from the brush border (microvilli, see Figure 3) split these chains into smaller and smaller molecules and individual amino acids that can then be absorbed.

Gluten: The Problem Protein

When most people think of protein, they think of meat, fish, eggs, and cheese, but protein is an essential part of many foods. And the protein that gives the small intestine of many people (with and without celiac disease) the most trouble is gliadin, the alcohol-soluble portion of gluten, which

is the protein portion of wheat and several other grains. It contains one fraction—a particularly large (thirty-three amino acids long) peptide chain—that is not readily digested. So despite all the grinding, churning, mixing, and battering of digestion, some proteins remain intact. It is this fraction of gliadin that is thought to cause celiac disease.

Fat

Fat is one of the main building blocks of the body, providing long-term energy stores and the cholesterol we need. Cholesterol is the main component of cell membranes and is needed to maintain the integrity of every cell in the body. Fat breakdown begins in the mouth and is continued in the stomach, but the actions of enzymes from the pancreas and the liver enable the small intestine to digest most of the fats we eat and absorb and transport them into the bloodstream.

Mineral and Vitamin Digestion

Specific minerals and vitamins are crucial to body growth, function, and metabolism. Even minor deficiencies disrupt body chemistry. Vitamins are either water or fat soluble. Water-soluble vitamins, the B family and C, move across the watery chyme quite easily, either on their own or assisted by special carriers. Fat-soluble vitamins must be emulsified to make the trip. Water, sodium (salt), calcium, iron, potassium, and other trace minerals are readily absorbed in different parts of the small intestine. Most require specialized porters to carry them across the brush border. If the villi are damaged and unable to produce and supply these shuttles, minerals and vitamins cannot be absorbed. Whatever is left of the chyme in the small intestine—mainly non-digestible fibers and fluid—is then pushed by peristalsis into the colon.

The Colon (Large Intestine)

The colon (large intestine) is about six feet long and the bottom end of the digestive tube. It acts as a receptacle for all the liquid and food products that do not get absorbed and prepares them to be eliminated by dehydrating and solidifying them into fecal matter. The main function of the colon is the absorption of water. As the food is pushed through the colon about two liters of water is absorbed back into the body. The fecal matter becomes more and more concentrated and then stored until it is eliminated through the rectum. The longer it takes to expel feces, the more water is absorbed, making the stool harder and, in turn, more difficult to expel. Diets high in fiber (raw fruits and vegetables, high-fiber cereals) create greater fecal bulk that goes largely unabsorbed by the small intestine and creates larger stools.

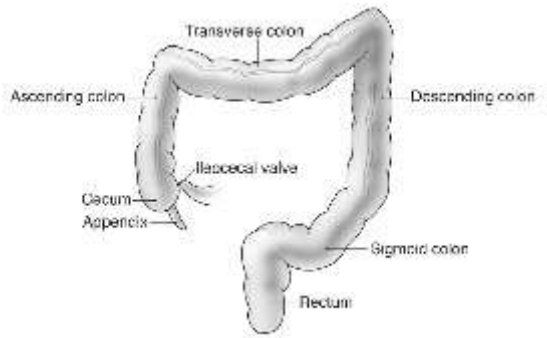


Figure 6. The Large Intestine

The colon is also inhabited by a large population of different bacteria that happily dine on and digest the unused fiber from our diet. Because of the slow movement of food in the colon, bacteria have ample time to multiply in this environment. About one-third of fecal matter is bacteria. These bacteria are beneficial because they produce vitamins, such as vitamin K. They also produce gas, a waste product of their own digestive process. Unlike the small intestine, which is controlled by involuntary muscles (occurring automatically), our brains and extrinsic nerves—facilitated by

stress, prunes, and opportunity—play a role in regulating the ano-rectal muscles.

When Normal Goes Pathological

With an understanding of the normal workings of the digestive system, it is easier to comprehend what happens when it gets broken. If the intestines do not contract properly as in diabetic neuropathy or scleroderma, there is impaired mixing of intestinal contents, which affects digestion and absorption. The lack of movement also means a higher rate of bacterial overgrowth (see Chapter 3) that can affect both the digestion and absorption of nutrients.

- You can do without a gallbladder, but a blocked bile duct, where bile cannot be released into the small intestine, results in the malabsorption of fats.
- If the pancreas is diseased, there may be no amylase to break up the larger carbohydrate molecules, lipase to break down fat, or trypsin to break down protein. (See Pancreatic Insufficiency, Chapter 16.)
- If the liver is diseased, the bile salts and fluids that digest fat are missing and transport of fats to and through the body is affected.
- If the intestinal villi are inflamed or destroyed, the digestion of food can be altered, disrupted, or completely halted. Food is maldigested and malabsorbed. It remains in the lumen, enters the colon, and causes diarrhea. And malabsorption feeds on itself—the lack of nutrients radiating throughout and eventually affecting the entire body.
- In a diseased state, the amount of fluid getting into the colon can exceed the capacity to absorb it and stool remains liquid. In addition, the products of digestion that were not absorbed (e.g., sugars, bile salts, fatty acids) stimulate the colon to secrete water. This causes more diarrhea. When the bacteria colonizing the colon act on the sugars, this can cause distention, cramps, and gas.

In Summary

The digestive system is a wonderfully meshed machine that turns the food we eat into nutrients that support all of the functions and systems of the body. And it is within the small intestine with its enormous absorptive surface that we find the focal point for the ultimate digestion, absorption, and transport of these nutrients. If the intestine is damaged in any way, or in multiple ways, we lose these mechanisms. The body is starved for the nutrients it requires to stay healthy. Diseases can upset any one, several, or all of the processes of digestion, absorption, transport, secretion, and contraction. Celiac disease is a disease of absorption.

2- The Digestive Tract in Flames: Celiac Disease

When the GI tract is functioning normally, we have no perception of digestion. Similarly, we cannot feel our blood circulate or our skin “breathe” unless there is something wrong with those processes. But when digestion is altered or interrupted, when the normal physiology breaks down, we usually know it. Unfortunately, the symptoms may not appear to match the problem.

Celiac Disease

Celiac disease—a multisystem disease in which the gastrointestinal tract is the major site of injury—is one of the most underdiagnosed hereditary autoimmune disorders. In an autoimmune disease, the body attacks itself. In the case of celiac disease, the body damages or destroys the villi (see Figure 4), the very components of the small intestine that enable us to absorb the nutrients we need to survive. And, much like a domino effect, the damage extends to other parts of the body as it progresses. The trigger for this destructive reaction is gluten, a group of proteins found primarily in wheat, rye, and barley. For those with celiac disease, the immune system treats gluten as a foreign body and inflames the villi of the small intestine in order to protect the body from the perceived invader. The villi, which enable the body to digest and absorb food, inflame

and eventually flatten. This can lead to a serious lack of vital nutrients. In some cases, the progress of the reaction is gradual, in others rapid and dramatic. While we know what triggers the immune response (gluten), the reasons why the response occurs only in certain genetically predisposed individuals and at varying times in their lives are still unclear.

What Is Gluten?

“It’s amazing that something as small as gluten can wreak such havoc with the body”. (Larry, 62)

Gluten is the term for the storage protein of wheat. Wheat is approximately 10 to 15 percent protein; the remainder is starch. Gluten is what remains after the starch granules are washed from wheat flour. The gluten fraction that is most studied in celiac disease is called gliadin, but there are other proteins that chemically resemble gliadin in rye (secalins) and barley (hordeins). These proteins are not strictly glutens, but are generally included in the term and are toxic to people with celiac disease. Most of the studies in celiac disease look at gliadin, but it is possible that there are other proteins in gluten to which people are sensitive. If you look at the grain table, you will see that the grass family has numerous branches. Wheat, rye, and barley—which contain gliadin, secalin, and hordein proteins, respectively—are closely related genetically. They come from similar tribes that also include spelt, kamut, and triticale.

Oats are on a different branch, closely related to rice, and are believed to be safe for most people (more than 98 percent) with celiac disease. Rice, corn, millet, sorghum, and several other grains are also safe. (For more on this subject, see Part IV.) Normally when we digest protein, it gets broken down in the stomach and small intestine into single amino acids or dipeptides (two amino acid molecules) that are readily absorbed by the small intestine. But the gluten molecule is resistant to the enzymes that break down proteins (peptidases). It is simply not digested well by humans. As a result, we are left with a long peptide chain, composed of thirty-three amino acids, that is called the toxic fraction of gliadin. This toxic fragment gets into the lining of the intestine, underneath the epithelial cells lining the villi. (See Figure 2.) And some people develop an immunological reaction to this gliadin fraction that starts to inflame and destroy the villi.

The small gluten fragments enter the bowel in both health and disease. It is believed that they enter between as well as through the cells. It may also be related to breaks in the mucosal barrier caused by an infection. It is also unclear how gliadin initiates the immune response and intestinal changes that lead to celiac disease. These areas are the subject of current research into the disease. (See Chapter 27.) What is understood is that the gliadin fraction is the main environmental trigger and culprit in the disease. It only becomes harmful when tissue transglutaminase (tTG) is activated. Essentially, celiac disease is an abnormal reaction to a normal food substance. So, while wheat may be the “staff of life” for some, for others it more closely resembles the “terminator.”

What Goes Wrong: The Role of Inflammation

As described in Chapter 1, the digestive system is constantly open to the bacteria, toxins, and foreign elements in our food and water supply. The system’s first line of defense is an intact mucosa—the lining of the entire GI tract. The second defense is the actions of gastric acid, which rid the system of many of the unwanted organisms that we might ingest. The third barrier erected by the digestive system is a limited, but constant level of inflammation that is present in the intestine, dealing with the potentially toxic environment. This controlled inflammation is one of the body’s initial immune responses and serves to seal off the infected area. The inflammation is caused by a family of white blood cells that are designed to protect the body from all types of toxins. These white blood cells produce antibodies (immunoglobulins, Ig) that target microbes. These immunoglobulins play an important role in helping the body to prevent or to get rid of infections. Of particular interest to the digestive system, IgA (immunoglobulin A) is made in abundance by the intestinal immune system and is secreted into both the lumen of the intestine

and the bloodstream. Fetuses receive IgG antibodies from the maternal blood as it crosses the placenta, and breast-fed children receive IgA antibodies through mother's milk.

These two sources of antibodies are important forms of protection for infants until their own immune systems have developed. When working properly, the inflammatory mechanisms and our immunological arsenal allow us to take in nutrients and keep unwanted food toxins, parasites, and bacteria out. But when the body senses an invasion of any kind, it responds to eliminate the problem. The normal level of inflammation increases as more and more inflammatory cells are attracted to the area "under attack." Each cell has a specific job. Many act as messengers, calling for reinforcements. As more "troops" are deployed to the area, damage occurs to the tissue that is being protected. The body's arsenal consists of a variety of white blood cells and inflammatory messengers that release chemicals to kill bacteria and unwanted materials and attract more inflammatory cells—which continues the inflammatory response. Macrophages, the scavenger cells of the immune system, are recruited to clean up the damage.

They engulf and destroy foreign matter, but they also liberate more enzymes that cause tissue damage. It is much like the scene of a fire after water and chemicals have extinguished the blaze and caused their own forms of residual damage. If production of these toxic products continues unchecked, not only are the foreign antigens destroyed, but normal tissues are damaged and normal regrowth and regeneration cannot occur. The actual substances that cause the damage are the cytokines, specifically a cytokine called interferon gamma. These protein messengers release chemicals that cause inflammation and flattening of the villi (villous atrophy). Villous atrophy is not specific to celiac disease; it is the main way the small intestine responds to any insult. (For more on research into blocking the cytokines as a treatment for celiac disease, see Chapter 27.) Finally, plasma cells in the inflamed tissue release antibodies in response to the inflammation and assault. These antibodies are specific to the pathogen or toxin they are fighting. By identifying these specific antibodies through blood tests, physicians can then determine the cause(s) and, therefore, the treatments for a disease or infection.

What Is Tissue Transglutaminase (tTG)?

In order to understand what is believed to be one of the key mechanisms that cause celiac disease, it is important to understand the role of tissue transglutaminase, or tTG. tTG is an important enzyme that is found in every tissue of the body. tTG acts by joining proteins together, a crucial part of wound healing and bone growth. But while tTG is continually acting to protect us, heal wounds, and get rid of damaged tissue, it also acts on gliadin, turning it into a more toxic molecule for people with celiac disease. It is believed that tTG converts the gliadin molecule into a form that interacts with and activates specific immune cells. This triggers an immune "recognition factor" in certain genetically prone individuals that sets off the inflammatory process that results in damage to the villi. Therefore, to have celiac disease, you need gliadin, tissue transglutaminase, and certain genes. As part of this interaction with gliadin, tTG gets incorporated into the white blood cells that are making antibodies to fight the inflammation. As a result, these cells produce antibodies to tTG. These antibodies are not thought to be responsible for the damage; they are thought to be a phenomenon that goes along with the process. Therefore, testing for antibodies to tTG is one highly specific way of testing for celiac disease.

The Intestinal Battlefield

When the immune system senses a serious infection or foreign invader, the normally controlled inflammatory process revs up. After repeated assaults, the inflammation causes the villi to atrophy (shrink) and eventually flatten, losing their absorptive power. The loss of the villi reduces the surface area available for absorption and destroys the enzymes in the microvilli responsible for the digestion and transport of nutrients. (Without the epithelial cell barrier, our immune system begins to make more antibodies to food proteins.) The inflammatory response resembles a battlefield with different troops racing to the scene, releasing their chemical weapons, and leaving

a great deal of damage and debris. Much as in any conflict, if there are only occasional skirmishes, there is not much ancillary damage, and the body can repair itself. This happens when we eat spoiled food, get a stomach “bug,” drink water with an unfamiliar local bacterium, and so forth. The body responds by putting in more inflammation. The inflammation deals with the problem, and then the body recovers. In the digestive tract of people with celiac disease, the gliadin molecule gets into the intestinal lining and continually stimulates the inflammatory response. The inflammation becomes excessive and causes continuous damage to the villi until the triggering toxin is removed.

The Digestive Tract in Flames

The digestive tract of people with celiac disease presents a pathological picture of:

- Villous atrophy (flattened villi).
- Crypt hyperplasia (the crypts, where the epithelial cells that cover the villi are made, work overtime but ineffectively, creating cells that cannot be used).
- Intense inflammatory reaction

Essentially, the body does not perceive that it is attacking itself, only a “foreign” protein in food. But the immunological reaction destroys the very thing it is trying to protect. The intestine will not recover until you interrupt the vicious cycle by taking gluten out of the diet. This allows the inflammation to abate and normal intestinal appearance to return. With the regrowth of the villi, function can return. Until then, the digestive system creates symptoms that reflect the level of damage to the body—it begins to ask or yell for help.

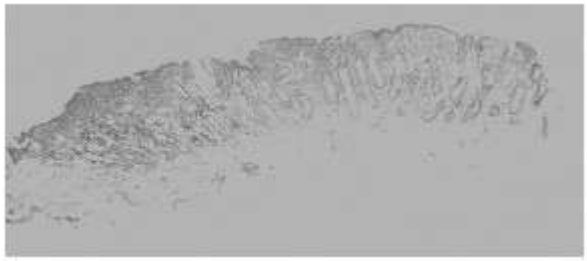


Figure 8. Biopsy Slide of Total Villous Atrophy

This biopsy slide was taken from an asymptomatic twenty-one-year-old female in whom blood tests for celiac disease were positive. They were taken because her mother was diagnosed with celiac disease.

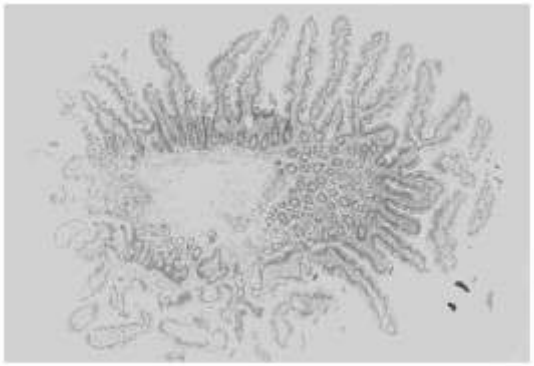


Figure 9. Biopsy Slide of Normal Villi

This normal duodenal biopsy shows long fingerlike villi with small, short crypts.

3- How Does Celiac Disease Affect You?

“I didn’t leave the house for six months; I had to be near the bathroom”. (Casey, 34)

“I never felt well, and I never felt sick enough to see a doctor”. (Marilyn, 28)

The symptoms of celiac disease may come on gradually or they may appear suddenly and dramatically. Symptoms may also wax and wane over a long period of time. Compounding the diagnostic challenge, there are approximately six “silent” or asymptomatic cases for each symptomatic one. Underlying the entire discussion is the medical question of what constitutes a symptom of celiac disease, since the definition is changing and covers a large spectrum of disorders.

“My daughter had vomiting and diarrhea starting in February. The pediatrician thought it was gastritis or reflux from February to July. We did neurological scans—he thought the vomiting was neurological, something with her balance. He sent me to a gastroenterologist who thought it looked like gastritis, did barium through the nose (an upper GI). Everything connected to gastritis or reflux. By July, she had lost eight pounds, lost her hair, and stopped walking. She had no more muscle on her legs. She had that distended belly like a starved child.... such a skinny neck.... and she started getting the black rings under her eyes and the black lips and the pediatrician kept saying, “You just have to go through this, a lot of kids vomit and have diarrhea, it’s no big deal.” My daughter weighed twenty-five and change at her two-year visit, and five months later, she was sixteen pounds. I told my husband I don’t think she’s going to make it.

The gastroenterologist discovered the celiac disease four days before we came to the hospital. I was told, “Just give her gluten-free foods, any store will know what you mean, she’ll be fine,” and he hung up on me. When she stopped moving, we drove in the middle of the night to the hospital and the resident told me if we’d waited a day longer she would have been dead. She was so severely dehydrated and malnourished. She was hospitalized and needed to stay on the feeding tube for eleven days. We had gotten so far into the disease that her intestines and her gut were just in such disrepair. We had to train her to walk again. I thought she was going to die. We finally took her home and cooked gluten-free foods for her. After one month, she gained seven pounds, she looked chubby, and her hair was growing in”. (Ilyssa, 33)

Celiac disease was once considered a “wasting” disease, specific to early childhood. The typical picture was a child of less than two years of age with malabsorption symptoms, including diarrhea, failure to thrive, muscle wasting, a distended belly (the textbook case), irritability, and sleep disturbance. Ninety percent of children with these symptoms—diarrhea and failure to thrive—are diagnosed with celiac disease within the first five years of life. Today, studies have shown that the majority of patients do not have “classic” celiac disease but a “silent” presentation. They either have minimal or no gastrointestinal (GI) symptoms, but suffer from related autoimmune diseases, complications from untreated celiac disease and/or the manifestations of malabsorption.

Most patients are diagnosed in their fourth to sixth decades of life and have symptoms for approximately nine years prior to diagnosis. Until the National Institutes of Health (NIH) Consensus Conference in 2004, celiac disease was classified as typical (the classic symptomatology described above) versus atypical (all nondiarrheal symptoms). There, experts from around the world concurred that atypical celiac disease was now the most common form of presentation and changed the medical terminology for the condition. It is hoped that this will also change the perception of the disease in the professional communities and shorten the time frame to diagnosis.

Severe or “Classic”

“I realized I had never cut (my daughter’s) nails in a year. I thought the nurse was cutting her nails, the nurse thought I was cutting them. In the hospital, going over all her symptoms, we realized no

one was cutting them: she had no nail growth". (Ilyssa, 33)

"Classic" celiac disease connotes mild to severe symptoms that predominantly involve the GI tract. The severity of intestinal symptoms is directly related to the amount of intestine that is damaged. Severe cases involve villous atrophy throughout much of the length of the small intestine and malabsorption affecting all nutrients. If the malabsorption is severe, it may result in dramatic weight loss and vitamin deficiency. Severe cases usually result in gastrointestinal disturbances, including diarrhea, cramps, bloating, lactose intolerance, increased reflux, and dyspepsia.

Atypical Celiac Disease

The inflammatory process and villous atrophy may involve only the upper part of the GI tract, and may or may not progress very far down the length of the small intestine. People with this condition may malabsorb a single nutrient such as iron or calcium in the proximal (upper) portions of the small intestine. This leads to associated conditions such as anemia, osteopenia, or osteoporosis. Many of these patients also have mild but persistent gastrointestinal symptoms such as reflux, bloating, and dyspepsia that often get labeled as irritable bowel syndrome (IBS).

"I was diagnosed in 1991. We had my daughter screened in 1993 because she was so very thin. Her test results were totally negative. In 1997, she was a college senior, at a good weight. To our surprise, she was diagnosed after participating in a family screening study. One of my sons was also tested at that family screening. He had no symptoms and the results were negative, as expected. A year and a half later, he was screened again as part of a family genetic study. We were all shocked when his antibodies were totally positive. Both my son and daughter were completely asymptomatic, yet their diagnosis was confirmed with positive biopsy results. I have another son who has recurrent GI (gastrointestinal) problems. He too has been screened twice and biopsied once, all with totally negative results. I was so surprised by the results of my children's screenings that I wrote an article—"Don't Try to Guess Who Is the Celiac in Your Family." (Sue Goldstein, founder of the Westchester Celiac Sprue Support Group)

Silent Celiac Disease

Some patients with silent celiac disease recognize their milder symptoms only retrospectively. The sense of fatigue that comes on after an illness or pregnancy and never seems to dissipate; dental enamel defects that are attributed to antibiotics; childhood irritability and illness. Some people exhibit no gastrointestinal symptoms due to the celiac disease itself until they develop a complication such as adenocarcinoma (cancer) of the small intestine. Patients also present with diabetes or anemia. Patients with silent celiac disease often appear later in life with symptoms of what are now understood to be related conditions such as dermatitis herpetiformis (an intensely itchy skin condition), peripheral neuropathies (numbness and tingling in the extremities), depression, or infertility. Because some patients are truly asymptomatic, it is important to understand that the malabsorption of nutrients is dangerous to one's general health. Many patients who do not have diarrhea think that there is no need for treatment. But the longer individuals have celiac disease, the more likely they are to get other autoimmune diseases. (See Chapter 14.) Even without any symptoms, patients need to be treated to prevent further damage.

Every Body Reacts Differently

It is not clear why some people get dermatitis herpetiformis and others neuropathies or migraines. Each body reacts idiosyncratically to the lack of certain vitamins or minerals as well as to the disease. The long-term effects of celiac disease also range from the silent to the severe. The four major categories of symptoms and complications are:

- Intestinal problems (diarrhea, flatulence, reflux, and pain and bloating)

- The manifestations of malabsorption (vitamin deficiency, iron deficiency, fatigue, calcium malabsorption leading to osteoporosis, and protein and calorie malnutrition causing weight loss and muscle atrophy)
- Systemic inflammatory reactions and autoimmune diseases
- Malignancies

Within each of these categories, the manifestations range from very mild to potentially life-threatening—but the reason for this variable expression of the disease is unclear.

Intestinal Problems

Diarrhea

“It started as an infant. I had to be on special formulas. I remember having to tell my mother when I made a “frankfurter”—as opposed to the diarrhea I usually had”. (Sara, 43)

Diarrhea is most commonly the result of infections, viruses, or toxins due to “food poisoning.” This diarrhea is self-limiting—once the body rids itself of the unwanted organisms or toxins, the intestines return to normal. In celiac disease, the diarrhea may come and go, but it usually recurs. “I had five episodes of gastroenteritis last year” is a common refrain. There are several mechanisms at work.

The Burn

What is going on in the intestines is much like what happens to skin that has been burned. When someone is badly burned, they lose fluid, serum, and protein through the inflamed, destroyed skin layers. When an individual has prolonged inflammation in the intestine, the epithelial cell barrier breaks down and loses its integrity, or barrier function. It is a two-way process—the intestine becomes permeable to substances that would not usually get absorbed, and the barrier to fluid loss is breached. The intestines “weep” or ooze serum (blood fluids). The medical term is protein-losing enteropathy. People lose the protein in their blood through weeping of serum. The loss includes that of surface area, villi, and microvilli.

Malabsorption

The second major cause of diarrhea is malabsorption. When sugars and fat are malabsorbed, they draw water into the colon. In a diseased state, the amount of fluid getting into the colon exceeds its capacity to absorb it and the stool remains liquid. In addition, the products of digestion that were not absorbed (for example, sugars, bile salts, and fatty acids) stimulate the colon to secrete water. The colon loses its function and secretes rather than absorbs liquid. All of the bacteria that inhabit the colon hungrily dine on the available sugars and fats, releasing gas and causing distention, cramps, and increased flatulence. Malabsorption can occur when any of the organs of the digestive system are diseased and disrupt digestion, absorption, or transport. When children present with a failure to thrive or with short stature, it is an indication of malabsorption. They get diarrhea more frequently than adults with celiac disease because their digestive tracts are shorter and they have less area to compensate for damage to the mucosa.

Crypt Hypertrophy

Diarrhea can also be contributed to by crypt hypertrophy, which causes increased water secretion. Water secretion occurs mainly in the crypts, water absorption in the villi. (See Figure 4.) There is usually a delicate balance. With the loss of villi and swelling of the crypts, the secretion far outweighs the absorption.

Lactose Intolerance

A lactase insufficiency or secondary lactose intolerance can cause diarrhea. Lactase, the enzyme that digests milk products, is produced in the microvilli or brush border of the epithelial cells; so if you lose surface area/epithelium, you lose those enzymes. A gluten-free diet will usually restore the enzymes as well as the villi.

Bacteria

Bacterial overgrowth is another contributory cause of diarrhea. Patients with celiac disease have more bacteria in their small intestine than usual. The mechanism is unclear but may be disturbed motility (movement in the digestive tract). The bacteria digest the "digesters," the enzymes, contributing to malabsorption and diarrhea. (For more, see Chapter 16.) Finally, the definition of diarrhea is sometimes questionable. It revolves around the concept of a "normal" bowel movement. The baseline for assessing a problem is what people are used to having. Most people are conditioned to have one per day. Some people are constipated normally. When stools become looser and more frequent than usual, that indicates something is happening—diarrhea. When stools are liquid, people have the sensation that more stool is waiting to be expelled, but nothing comes out; or more comes out, and the sensation persists. The medical term is tenesmus—a feeling of incomplete evacuation. This commonly occurs with colitis and irritable bowel syndrome (IBS), but it can occur with any cause of diarrhea.

Flatulence

"I had no symptoms, but a lot of gas. I thought it was a family trait. My mother and brother had it". (Sandy, 38)

Another common intestinal problem is flatulence. Gas is created by the fermentation of food products in the intestine. It is perfectly normal and generally odiferous, and it's often treated with humor or embarrassment. Doctors who have researched the phenomenon and published data on the subject report that people pass gas (flatus), on average, ten times each day, and passage of gas of up to twenty times daily is still considered normal. While this may be more information than some people require, it is important to note that people are more gassy on a high-fiber diet and when they malabsorb sugars, as in lactose intolerance. There is currently no research on how often someone with celiac disease passes gas.

Reflux

"The acid and pain was horrendous; I used to eat Rolaids for dinner. I tried saltines, Cream of Wheat, graham crackers. I was doing myself in—and thinking I was doing the right thing". (Anna, 40)

Reflux, or GERD (gastroesophageal reflux disease), is quite common. It is estimated that 20 percent to 40 percent of the population regularly have heartburn, the most common symptom of reflux. It is the main reason people buy over-the-counter antacids. People with celiac disease have an increased tendency to get heartburn. This is due to a gastric motility (muscle movement) problem. The stomach does not empty properly and the contents tend to reflux (to flow back up the esophagus). This is aggravated by a reduced lower esophageal sphincter tone (the one-way valve through which food travels from the esophagus into the stomach), which predisposes the stomach contents to reflux. Some patients report that their reflux and heartburn improve on a gluten-free diet.

Pain and Bloating

"I would eat a meal and blow up—literally. I looked eight months pregnant. It was like someone

pumped me full of gas. Oh, you cannot believe the pain. It got worse when we went to Italy. All that great bread and pasta—I was doubled over. I couldn't button my pants". (Ingrid, 52)

People with excess gas, diarrhea, or reflux experience varying degrees of pain and bloating. They are the classic symptoms of stomach and/or intestinal distress, otherwise known as dyspepsia. They are common signs of lactose intolerance, irritable bowel syndrome, malabsorption, obstruction, and many other intestinal problems. People may experience these symptoms because of celiac disease.

The Manifestations of Malabsorption

While intestinal problems (diarrhea and flatulence) were once considered to be the major manifestations of celiac disease, the more remote effects of malabsorption are now understood to be the most common symptoms seen by doctors. The ability of the small intestine to compensate for malabsorption in one section is at once remarkable and specifically limited. Fat and sugars are absorbed mainly in the proximal intestine. As explained earlier, when they are malabsorbed, they get into the colon, causing diarrhea. But many people do not get diarrhea because the last third of the small intestine, the ileum, can absorb fats and sugars and can compensate for damage in the duodenum and jejunum.

Vitamins and Minerals

These nutrients are absorbed only in specific sections of the small intestine. Vitamin B12 is absorbed in the ileum, so it is not common for people with celiac disease to have vitamin B12 malabsorption. Iron, much of our calcium, fat-soluble vitamins, and folic acid get absorbed in the proximal portion of the small intestine, where celiac disease does much of its damage. Therefore, most people with celiac disease will have bone problems ranging from osteopenia to osteoporosis because of calcium malabsorption, and low ferritin (the form that iron takes when stored for usage in the body), indicating iron deficiency. The potential for vitamin and mineral deficiency is one of the reasons it is important for all patients diagnosed with celiac disease to see a nutritionist/dietician. The chart that follows outlines the fat-soluble vitamins commonly malabsorbed in celiac disease. It also outlines their function and their effect on the body.

Fat-soluble-vitamins

Vitamin A function: Plays an essential role in vision and retinal function; necessary for sexual reproduction, normal growth, bone development, growth of epithelial tissue, and the immune system. Deficiency can cause anemia and reproductive, vision, and growth problems. Severe deficiencies can result in inhibited growth, night blindness, and loss of the sense of taste. Excess amounts of vitamin A can be toxic.

Vitamin D function: Important factor in the intestinal absorption of calcium and bone growth. Deficiency causes rickets (soft, deformed bones) in children and can contribute to calcium and bone problems (osteopenia and osteoporosis) in adults. Excess amounts can be toxic; supplements should be monitored.

Vitamin E function: An antioxidant that protects cells from damage. Deficiency has been associated with neurological problems, such as peripheral neuropathy and ataxia, and anemia. There is concern that excess amounts can be toxic.

Vitamin K function: Aids in blood clotting. Anticoagulant drugs such as Coumadin prevent coagulation by blocking the actions of vitamin K. Deficiency results in impaired synthesis of clotting factors in the liver. In turn, bruising and easy bleeding occur.

The fat-soluble vitamins are absorbed with other fats in the proximal intestine and require bile and

pancreatic secretions to be properly digested. They are malabsorbed when the small intestine or interacting organs of digestion (the pancreas, liver, or bile ducts) are impaired. Levels of vitamins A and D can be measured and should be checked if specific symptoms warrant a closer inspection.

Anemia

“For years I was anemic. Doctors said: “You have your period, you don’t eat right.” So, I would take iron and it would make me sick. I was constipated and having abdominal pain. There were points I couldn’t take it anymore”. (Lori, 31)

The body stores iron in the liver and bone marrow as a molecule called ferritin. Iron is extremely important to the body, helping to carry oxygen in the blood and aiding in energy production, cellular respiration, and immune function. When iron stores are depleted—due to blood loss and/or malabsorption—and not replaced through the diet, you become anemic. The consequences have a large impact on bodily function. There are three kinds of anemia:

- Microcytic (small red blood cells; most often due to iron deficiency).
- Normocytic (red cells normal size; most often due to chronic illness and inflammation).
- Macrocytic (red cells larger than normal; most often due to vitamin B12 or folic acid deficiency).